

REMARKS

Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are pending in the application. Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 were rejected. Claims 4-6, 11-13, 17, 20, 23 and 25 were subject to a restriction requirement and were canceled in the prosecution. No claims have been allowed.

Claim Rejections- 35 U.S.C. §103

1. Claims 1-2, 7-9, 14-16, 18-19 and 21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Sigal et al. (U.S. Patent No. 6,319,670 B1).

Kim et al. discloses a conductimetric membrane strip immunosensor for the detection of human serum albumin (HSA) as an analyte. Kim et al. teaches the use of antibodies against the HSA analyte which have been conjugated to colloidal gold particles as a signal generator for the conductimetric immunosensor. Kim et al. teaches first to affinity purify antibodies against human serum albumin (HSA) and then to conjugate the

affinity purified antibodies with colloidal gold particles. Kim et al. adds polyaniline strands to the gold particles to improve electrical conduction.

Sigal et al. disclose methods for performing electrochemiluminescence assays using electrically conductive microparticles having a first assay-ligand (such as an antibody) immobilized on its surface. A second assay-ligand (such as an antibody) is immobilized on an electrode surface. The antibodies can each bind an analyte of interest so as to form a complex, thereby binding the electrically conductive complex to the electrode surface. Thus, the conductive microparticles are bound directly to the electrodes. Sigal et al. do not teach a biosensor device similar to the claimed invention. The microparticles taught by Sigal et al. can have a wide variety of sizes and shapes. According to Sigal et al., "[t]he particles may be spherical, oblong, rod-like, etc., or they may be irregular in shape." (Sigal et al.: col. 5, lines 33-38). According to Sigal et al., "[m]icroparticles of the invention may also include macromolecules or aggregates thereof (e.g., a polymer, a dendrite, a polysaccharide, a protein, nucleic

acids, or other biological macromolecules of appropriate size)." (Sigal et al.: col. 5, lines 51-55).

Independent claims 1, 7, 8 and 14 are limited to "an electrically conductive polymer formed by oxidative polymerization of monomers, and the polymer has been mixed to react with the second capture reagent to form a conjugate, wherein there is an absence of electrically conductive particles". The claim language limits the conductive polymers to be formed in absence of conductive particles, and formed by polymerization of monomers. In addition, the claim is amended to clarify that the second capture reagent is directly bound to the electrically conductive polymer to form a conjugate. Support for this is found at page 16, lines 12-19.

Kim et al. also synthesized polyaniline by oxidative polymerization (Kim et al.: page 909, left column, first full paragraph) to form "strands" of polymer (Kim et al.: page 913, last paragraph and page 914, first full paragraph) as "extended filaments" (Kim et al.: page 913, right column, last paragraph). Thus, it is clear that conductive polymers formed by oxidative polymerization of monomers are not particulate, but are

extended filaments directly bound to the capture reagent as a conjugate. However, while Kim et al. uses polyaniline as the polymeric conductor molecule, Kim et al. introduced the polymeric conductor molecules indirectly on the particulate gold surface after combining the antibody solution with the gold particles for conjugation. (Kim et al.: page 909, left column, first full paragraph).

According to M.P.E.P. §2144.04 II. B., the omission of an element with retention of the element's function is an indicia of unobviousness. *In re Edge*, 359 F.2d 896, 149 USPQ 556 (CCPA 1966). The claims at issue in *In re Edge* were directed to a printed sheet having a thin layer of erasable metal bonded directly to the sheet wherein said thin layer obscured the original print until removal by erasure. The prior art disclosed a similar printed sheet which further comprised an intermediate transparent and erasure-proof protecting layer which prevented erasure of the printing when the top layer was erased. The claims were found unobvious over the prior art because the although the transparent layer of the prior art was eliminated, the function of the transparent

layer was retained since appellant's metal layer could be erased without erasing the printed indicia. In the presently claimed device and system, the gold particles of Kim et al. are removed while maintaining the conductive properties of the gold particles.

In addition, it is improper to combine references where the references teach away from their combination. *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). Kim et al. teach the strategy of using the colloidal gold-antibody conjugates with the conducting polymer and not the direct labeling of the antibody with the conducting polymer by chemical reaction "because, in such a case, the protein molecule itself does not contain available sites for electron relay." (Kim et al.: Conclusions, page 914). Therefore, one skilled in the art reading Kim et al. would be directed away from eliminating the metal (gold) particles since Kim et al. teaches that direct labeling of the antibody with the polymer would not have the electron relay sites on the antibody protein molecule which are necessary for conduction. Therefore, Kim et al. and Sigal et al., either taken alone or in combination, do not show or

suggest the biosensor device and system of the presently amended claims. Reconsideration of the rejection is requested.

2. Claims 3, 10, 22, 24 and 26 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (*Biosensors & Bioelectronics* (2000), vol. 14, pp. 907-915) in view of Sigal et al. (U.S. Patent No. 6,319,670 B1) as applied to Claims 1, 8 and 14, and further in view of Roberts et al. (U.S. Patent No. 5,958,791).

Claims 22, 24 and 26 are directed to a device or system, wherein the biosensor device is a multi-array device comprising: a plurality of first zones on the single strip of substrate, each of the first zones having a first capture reagent with a different specificity bound to the single strip of substrate between electrodes to immobilize one of multiple analytes on the single strip of substrate so that each of the multiple analytes can be detected simultaneously from the sample on the single strip of substrate of the multi-array biosensor device. The multiple analytes can be detected simultaneously, as

claimed in the system of Claim 26, by providing a constant current and measuring the generated voltage signals which are proportional to the resistances across each of the first zones. Support for these limitations is found in Example 2 on page 19, lines 15-29 of the specification, describing Figures 3 and 4.

Claims 3, 10, 22, 24 and 26 are patentable over Kim et al. and Sigal et al. for the reasons discussed above. Additionally, with regards to Claims 22, 24 and 26, Kim et al. and Sigal et al. further fail to teach a multiple array of first zones as claimed, so that multiple analytes are detected simultaneously on a single strip of substrate. Roberts et al. teaches test devices including multiple sets of interdigitated electrode arrays for simultaneous multiple analyte detection and assay of a test sample for a plurality of analytes. However, Roberts et al. does not teach a multi-array on a single strip of substrate as claimed and as illustrated in Figure 3. The simultaneous multiple analyte detection taught by Roberts et al. uses multiple sets of interdigitated electrode arrays, each mounted on separate strips of substrate (absorbent material 112), in order to

perform simultaneous multiple analyte detection to assay the test sample for a plurality of analytes. The liposome-enhanced immunoassay and test device taught by Roberts et al. would not suggest to a person of ordinary skill in the art the single multiple array as taught by Applicants, since the nature of the immunoassay and test device taught by Roberts et al. requires separate competitive binding portions 104 and measurement portions 106.

The test of Roberts et al. requires that a test mixture with the analyte of interest first passes through a competitive binding portion 104 having the binding material for the analyte before passing through a liposome lysing portion 106 where a liposome lysing agent releases the electroactive marker from the liposome. The electroactive marker is then carried by the migrating mixtures, via capillary action, into and through the electrochemical measurement portion to complete the electrical circuit (Roberts et al.: col. 15, line 53 through col. 16, line 5). Each of these must be performed on separate strips of absorbent material 112. A multi-array on a *single* strip of substrate as claimed

by Applicants (seen illustrated in Figure 3) wherein a plurality of analytes in a mixture can each be individually detected at one of the multiple regions 21A to 21D would not be suggested by the cited prior art references. As seen in Figure 3, each one of the analytes bind to a specific capture reagent/antibody at one of the multiple zones between the electrodes on a single strip to generate a signal at one of the regions 21A-21E representative of that particular analyte. Each analyte will generate one of an array of simultaneous voltage signals 33 which is proportional to the change of the resistance in that region. The immunoassay and test device taught by Roberts et al. does not show or suggest such a multi-array, since specific binding must be completed *before* the test mixture flows between the electrodes in the measurement portion 106. If the adjacent electrodes are spaced too closely together in the immunoassay and test device taught by Roberts et al., the electroactive marker diffuses over to an adjacent region to generate a false signal in that region. Due to this problem, the electrode arrays of Roberts et al., unlike those arrays taught by Applicants, must be


maintained at a large enough distance so that no electroactive markers can diffuse over the electrodes in an adjacent measurement portion 106. This is the reason that a single strip of substrate can not be used.

The design of the device taught by Applicants does not have this problem with cross over signal, thus can be performed upon a single strip of substrate. Since only the first capture reagent specific for the one analyte to be detected is present between the electrodes, only the complex of the specific analyte to be detected and the second capture reagent bound to the electrically conductive polymer can be bound between the electrodes. Therefore any signal measured across the electrodes of any of the regions 21A to 21D is generated by specific binding of the desired analyte to the region. This can all be accomplished with a sample provided on a single strip of substrate. The cited references, taken alone or in combination, do not show or suggest such a multi-array device. The claims are therefore patentable over Kim et al., in view of Sigal et al., and further in view of Roberts et al. Reconsideration of the rejection is requested.

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In light of the above, it is now believed that Claims 1-3, 7-10, 14-16, 18, 19, 21, 22, 24 and 26 are patentable and in condition suitable for allowance. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,



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